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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 022052-000700US

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Signature _____

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Application Number	Filed
09/844,281	Apr. 30, 2001

First Named Inventor: Mangold

Art Unit	Examiner
1645	Graser, J.E.

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration number 44,461
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Signature

Kawai Lau
Typed or printed name

425-681-1833
Telephone number

January 14, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of _____ forms are submitted.

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TOWNSEND and TOWNSEND and CREW LLP

By: _____
Kawai Lau

PATENT
Attorney Docket No.: 022052-000700US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 1022
Beverly L. Mangold, et al.	Examiner: GRASER, J.E.
Application No.: 09/844,281	Technology Center/Art Unit: 1645
Filed: April 30, 2001	REASONS IN SUPPORT OF PRE-APPEAL BRIEF REQUEST FOR REVIEW
For: ANTHRAX SPECIFIC ANTIBODIES	
Customer No.: 70680	

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The reasons provided herein are in support of the Pre-Appeal Brief Request for Review (form PTO/SB/33) submitted herewith, which is in reply to the "final" Office Action mailed July 12, 2007, which set October 12, 2007 as the initial deadline for response. Therefore, a Petition for a three-month extension of time until Saturday, January 12, 2008 is enclosed herewith, and this submission, filed Monday, January 14, 2008, is believed to be timely filed.

A Notice of Appeal and the necessary fee of $255.00 are submitted herewith.

Reconsideration in light of the following reasons is respectfully requested.

Alleged rejection under 35 U.S.C. 112, first paragraph

The alleged rejection of claims 66-77 and 79-91 under 35 U.S.C. 112, first paragraph, fails to be both factually and legally supported. The allegation that the specification only enables a deposited antibody is misplaced and may be properly withdrawn.

The instant rejection fails to recognize two simple facts regarding the instantly claimed invention and the content of the application as filed. The first fact is that the rejected claims feature a monoclonal antibody that specifically binds spores and vegetative cells of *B. anthracis* but not the spores or vegetative cells of four other *Bacillus* species including *B. licheniformis*. This feature of the claims reflects the novelty of the claimed subject matter, which is supported by the fact that there is only a misplaced allegation of anticipation as explained below.

This feature also reflects the unexpected nature of the claimed subject matter because the antibodies which have this specificity were found to bind the EA1 polypeptide of *B. anthracis*. This additional feature is explicitly recited in rejected claims 66-77 and 79-84. The unexpected nature of this discovery is supported by the presence of significant similarity and identity between the *B. anthracis* EA1 polypeptide and the OlpA polypeptide of *B. licheniformis* as reported by the cited Mesnage et al document (see Figure 4 and page 1149 of that document). Because of the similarities and homology, there was no expectation of an antibody having specificity for *B. anthracis* relative to *B. licheniformis by binding EA1 polypeptide*.

But instead of recognizing this fact, the statements on pages 3-4 of the "final" Office Action, mailed 7/12/07, erroneously construes Applicants' past statements and alleges "that antibodies which bind EA1 would have cross-reactivity with OlpA of *B. licheniformis*." Applicants respectfully, but strenuously, disagree because the previous statements of July 21, 2006 merely point out the factual possibility of an antibody that binds EA1 polypeptide of *B. anthracis* but **does not** have the specificity for spores and vegetative cells of *B. anthracis* as featured in the claims This is supported by a simple review of Figure 4 in the cited Mesnage et al. document, which would lead the skilled person to expect an antibody being **non**-specific for EA1 relative to OlpA, and therefore **non**-specific for *B. anthracis* relative to *B. licheniformis*.

But this expectation does not alter a second factual oversight, which is that the instant application discloses both antibodies that **are** specific for *B. anthracis* relative to *B. licheniformis* and other *Bacillus* strains as recited in the claims (see pages 18-20, Tables 2-4) and a clear method for producing them. The methods in the Example on pages 10-12 of the instant application clearly set forth a protocol that can be followed repeatedly to produce additional monoclonal antibodies, which can be tested, or screened, as disclosed therein to identify those with the specificity recited in the claims.

This fact brings in the legal deficiency of the instant rejection, which is that the facts and legal standard in *In re Wands* (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), holding that claims

directed to antibody based methods did satisfy the enablement requirement) support the presence of enablement in the instant application. In both cases, there is a clear method for making and testing antibodies for the desired binding specificity. The "considerable direction and guidance;" "high level of skill in the art;" and "methods needed to practice the invention" present in the *Wands* case are also present in the instant application. So like the situation in the *Wands* case, no undue experimentation is required to make and use antibodies as featured in the instant claims.

But instead of recognizing the presence of enablement, the instant rejection improperly asserts a requirement for the claims "to recite the specific epitope by SEQ ID NO. to which the antibodies bind" (see page 5 of the "final" Office Action mailed 7/12/07). Applicants respectfully submit that U.S. patent law does not include such a requirement.

Moreover, the instant rejection alleges "unpredictability in using a monoclonal antibody which binds EA1 for detection of B. anthracis" (see page 6 of the "final" Office Action mailed 7/12/07). But this misses the feature of the pending claims, which is that a monoclonal antibody which has the necessary specificity relative to four (4) other Bacillus strains is used. The argument also misses the fact that the instant application clearly discloses methods to produce monoclonal antibodies and screen them for the required specificity. No more is needed for full enablement under *Wands* and well settled U.S. patent law.

Finally, the instant rejection is legally deficient because it is contradicted by the rejections, addressed below, alleging that it would have been obvious to make and use the claimed subject matter asserted as non-enabled. But the rejections alleging obviousness are not limited to the single monoclonal antibody alleged as enabled. Instead, the allegations of obviousness encompass all possible anti bodies encompassed by the claims. Therefore, Applicants point out that the rejections are contradictory and cannot be simultaneously asserted.

Alleged rejection under 35 U.S.C. 103(a)

The alleged rejection of claims 66-77, 79-91, and 93-96 under 35 U.S.C. 103(a) based on Mesnage et al., Kohler et al., and Loomis et al. fails to be both factually and legally supported. The allegation that the claimed subject matter is obvious is misplaced and may be properly withdrawn.

The most significant factual mistake in the instant rejection is the allegation that "a Western blot assay suggested that the antibodies [of Mesnage et al.] were highly specific to B. anthracis and did not cross-react" (see page 8 of the "final" Office Action mailed 7/12/07). But as noted on page

15 of Applicants' response of July 20, 2006, Mesnage et al. fail to teach or suggest any specificity relative to other *Bacillus* species. Instead, specificity was only noted relative to the sap protein of *B. anthracis*.

Another significant factual mistake is the allegation that "[t]here are no structural differences between the prior art antibody" of Mesnage et al. (see page 10 of the "final" Office Action mailed 7/12/07) and those of the claimed subject matter. Applicants respectfully point out that the relationship between function and structure in an antibody means that the functional features of the claimed subject matter require the antibodies to have distinct structures necessary to have the recited function(s). Applicants respectfully point out that there is no *per se* bar against functional limitations, and no *per se* requirement for particular structural features in a claim.

As for the legal deficiency, Applicants point out that the instant rejection alleges that the Mesnage et al. antibodies "would *inherently possess* the same binding capabilities" (emphasis added, see page 12 of the "final" Office Action mailed 7/12/07) as the antibodies of the claimed subject matter. The rejection also alleges that an anti-EA1 monoclonal antibody "would *inherently* have the ability to bind both spores and vegetative cells" (emphasis added, see page 14 of the "final" Office Action mailed 7/12/07). This last assertion reflects an apparent misapprehension of antibodies and epitopes, since the same EA1 polypeptide present on both spores and vegetative cells do not necessarily present the same epitopes in both situations. Therefore, the assertion is incorrect to the extent that it assumes knowledge in the art of identical epitopes without benefit of Applicants' own discoveries.

Applicants respectfully submit that this indicates that the instant rejection is improperly based on inherency, which cannot support a *prima facie* case of obviousness. Instead, there must be a reasoned explanation for why the skilled person in the field would make monoclonal antibodies based upon the polyclonal antibodies of Mesnage et al. with a reasonable expectation of success in arriving at the claimed invention **and** without reliance upon improper hindsight reconstruction.

Applicants point out that the similarities and identities between *B. anthracis* EA1 and the OlpA polypeptide of *B. licheniformis*, as reported by Mesnage et al., remove any expectation of success in making the monoclonal antibodies of the claimed invention. And the reliance on inherency reflects an improper reliance on Applicants' discovery to reconstruct the claimed invention by improper hindsight.

The alleged rejection of claims 66, 68 and 70-85 under 35 U.S.C. 102(b) or 103(a), based on Ezzell et al. fails to be both factually and legally supported. The allegation that the claimed subject matter is anticipated or obvious is misplaced and may be properly withdrawn.

The first factual error in this rejection is that Ezzell et al. teach "[m]ouse monoclonal antibodies to EA1" (see page 15 of the "final" Office Action mailed 7/12/07). Applicants point to their statements in the response filed April 26, 2007 (see pages 12-13 therein) regarding Ezzell et al.'s report of the antibodies binding "nonencapsulated cells" without any indication of the antibodies binding *B. anthracis* spores. But *B. anthracis* vegetative cells are encapsulated!

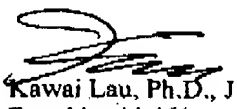
The second factual error is that an anti-EA1 monoclonal antibody "would *inherently* have the ability to bind both spores and vegetative cells" (emphasis added, see page 18 of the "final" Office Action mailed 7/12/07). As explained above, the same EA1 polypeptide present on both spores and vegetative cells do not necessarily present the same epitopes in both situations. Additionally, the Ezzell et al. antibody that allegedly binds nonencapsulated vegetative cells does not necessarily bind encapsulated vegetative cells. Therefore, the assertion is incorrect to the extent that it assumes the same binding properties between the Ezzell et al. antibody and those of the instant claims.

Moreover, the factual errors make the rejections are legally deficient because there is no teaching or suggestion of an antibody with the claimed characteristics and no expectation of success in making and using such an antibody as explained on pages 12-13 of the response filed April 26, 2007.

The alleged rejection of claims 67 and 69 under 35 U.S.C. 103(a) based on Ezzell et al. and Loomis et al. fails to be both factually and legally supported for the reasons provided above with respect to Ezzell et al. alone. Therefore, the allegation that the claimed subject matter is obvious is misplaced and may be properly withdrawn.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 425-681-1833.

Respectfully submitted,



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